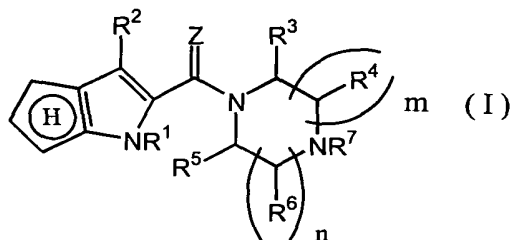
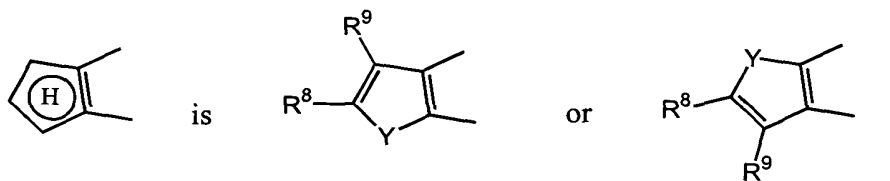


What is claimed is:

1. A compound of formula (I):



- 5 wherein



Y is O or S;

Z is O or S;

- 10 n is 1 or 2;

m is 1 or 2;

n + m is 2 or 3;

R<sup>1</sup> is H or C<sub>1-6</sub>alkyl;

R<sup>2</sup> is H, F, Cl, Br or C<sub>1-6</sub>alkyl;

- 15 R<sup>3</sup> and R<sup>4</sup> are, independently, H, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>1-4</sub>alkyl(C<sub>3-6</sub>cycloalkyl), cyano, -CF<sub>3</sub>, -(CO)NR<sup>p</sup>R<sup>q</sup>, -(CO)OR<sup>r</sup>, -CH<sub>2</sub>NR<sup>p</sup>R<sup>q</sup> or -CH<sub>2</sub>OR<sup>r</sup>; where R<sup>p</sup>, R<sup>q</sup> and R<sup>r</sup> are independently selected from H, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, phenyl, -C<sub>1-2</sub>alkyl(C<sub>3-6</sub>cycloalkyl), benzyl or phenethyl, or R<sup>p</sup> and R<sup>q</sup> taken together with the nitrogen to which they are
- 20 attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC<sub>1-6</sub>alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;
- 25 R<sup>5</sup> and R<sup>6</sup> are, independently, H or C<sub>1-6</sub>alkyl;

$R^7$  is  $-R^a$ ,  $-R^bR^a$ ,  $-R^e-O-R^a$  or  $-R^e-N(R^c)(R^d)$ , where  $R^a$  is H, cyano,  
 $-(C=O)N(R^c)(R^d)$ ,  $-C(=NH)(NH_2)$ ,  $C_{1-10}$ alkyl,  $C_{2-8}$ alkenyl,  $C_{3-8}$ cycloalkyl,  
 $C_{4-7}$ heterocyclic radical or phenyl, where the  $C_{4-7}$ heterocyclic radical is  
 attached at a carbon atom and contains one of O, S, NH or  $NC_{1-4}$ alkyl,  
 5 and optionally an additional NH or  $NC_{1-6}$ alkyl in rings of 5 or 6 or 7  
 members, where  $R^b$  is  $C_{1-8}$ alkylene or  $C_{2-8}$ alkenylene, where  $R^e$  is  
 $C_{2-8}$ alkylene or  $C_{2-8}$ alkenylene, where  $R^c$  and  $R^d$  are each independently  
 H,  $C_{1-4}$ alkyl,  $C_{2-4}$ alkenyl,  $C_{3-6}$ cycloalkyl or phenyl, or  $R^c$  and  $R^d$  taken  
 together with the nitrogen to which they are attached, form a 4-7  
 10 membered heterocyclic ring with 0 or 1 additional heteroatoms selected  
 from O, S, NH or  $NC_{1-6}$ alkyl, and where any phenyl or alkyl or cycloalkyl  
 moiety of the foregoing is optionally and independently substituted with  
 between 1 and 3 substituents selected from  $C_{1-3}$ alkyl, halo, hydroxy,  
 amino, and  $C_{1-3}$ alkoxy;  
 15 alternatively,  $R^7$  may be taken together with an adjacent  $R^4$  as well as  
 their carbon and nitrogen of attachment to form a 5, 6 or 7 membered  
 heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S,  
 NH or  $NC_{1-6}$ alkyl, and optionally and independently substituted with  
 between 1 and 3 substituents selected from  $C_{1-3}$ alkyl, halo, hydroxy,  
 20 amino, and  $C_{1-3}$ alkoxy;  
 $R^8$  and  $R^9$  are, independently, H, F, Cl, Br, I,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  
 $-C_{3-6}$ cycloalkyl,  $-OC_{3-6}$ cycloalkyl,  $-OCH_2Ph$ ,  $-CF_3$ ,  $-OCF_3$ ,  $-SCF_3$ ,  $-(C=O)R^k$   
 (wherein  $R^k$  is H,  $C_{1-4}$ alkyl,  $-OH$ , phenyl, benzyl, phenethyl or  $C_{1-6}$ alkoxy),  
 $-(N-R^t)(C=O)R^k$  (where  $R^t$  is H or  $C_{1-4}$ alkyl),  $-(N-R^t)SO_2C_{1-4}$ alkyl,  
 25  $-(S(=O)_p)-C_{1-4}$ alkyl (wherein  $p$  is 0, 1 or 2), nitro,  $-SO_2NR^lR^m$  (wherein  $R^l$   
 and  $R^m$  are independently selected from H,  $C_{1-4}$ alkyl, phenyl, benzyl or  
 phenethyl, or  $R^l$  and  $R^m$  taken together with the nitrogen to which they are  
 attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional  
 heteroatoms selected from O, S, NH or  $NC_{1-4}$ alkyl),  $-(C=O)NR^lR^m$ , cyano  
 30 or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing  
 is optionally and independently substituted with between 1 and 3  
 substituents selected from  $C_{1-3}$ alkyl, halo, hydroxy, amino, and  $C_{1-3}$ alkoxy;

and enantiomers, diastereomers and pharmaceutically acceptable salts and esters thereof,

with the following provisos,

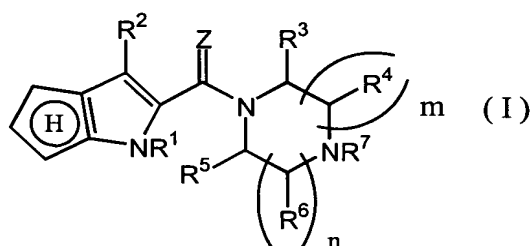
that  $R^6$  adjacent to N must be H where  $R^4$  adjacent to N is other than H,

5 that  $R^7$  is not  $-\text{CH}_2\text{CH}_2\text{OH}$ ; and

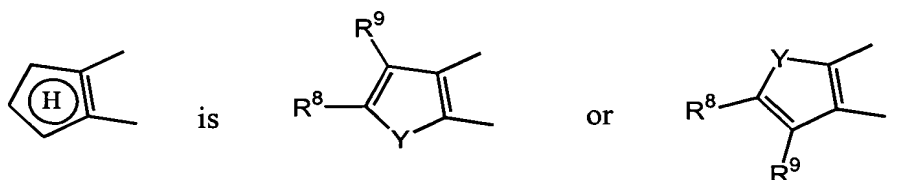
that where the core molecule is a 4*H*-furo, then one of  $R^4$  and  $R^6$  adjacent to N must not be methyl when the other is hydrogen unless  $R^6$  and  $R^4$  are taken together to form a bridging moiety.

2 A pharmaceutical composition containing a compound of formula (I):

10



wherein



15 Y is O or S;

Z is O or S;

n is 1 or 2;

m is 1 or 2;

n + m is 2 or 3;

20  $R^1$  is H or  $\text{C}_{1-6}$ alkyl;

$R^2$  is H, F, Cl, Br or  $\text{C}_{1-6}$ alkyl;

$R^3$  and  $R^4$  are, independently, H,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,

$\text{C}_{1-4}$ alkyl( $\text{C}_{3-6}$ cycloalkyl), cyano,  $-\text{CF}_3$ ,  $-(\text{CO})\text{NR}^p\text{R}^q$ ,  $-(\text{CO})\text{OR}^r$ ,  $-\text{CH}_2\text{NR}^p\text{R}^q$  or  $-\text{CH}_2\text{OR}^r$ ; where  $R^p$ ,  $R^q$  and  $R^r$  are independently selected from H,

25  $\text{C}_{1-4}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl, phenyl,  $-\text{C}_{1-2}$ alkyl( $\text{C}_{3-6}$ cycloalkyl), benzyl or phenethyl, or  $R^p$  and  $R^q$  taken together with the nitrogen to which they are

attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC<sub>1-6</sub>alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;

5 R<sup>5</sup> and R<sup>6</sup> are, independently, H or C<sub>1-6</sub>alkyl;

R<sup>7</sup> is -R<sup>a</sup>, -R<sup>b</sup>R<sup>a</sup>, -R<sup>e</sup>-O-R<sup>a</sup> or -R<sup>e</sup>-N(R<sup>c</sup>)(R<sup>d</sup>), where R<sup>a</sup> is H, cyano, -(C=O)N(R<sup>c</sup>)(R<sup>d</sup>), -C(=NH)(NH<sub>2</sub>), C<sub>1-10</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>3-8</sub>cycloalkyl, C<sub>4-7</sub>heterocyclic radical or phenyl, where the C<sub>4-7</sub>heterocyclic radical is

10 attached at a carbon atom and contains one of O, S, NH or NC<sub>1-4</sub>alkyl, and optionally an additional NH or NC<sub>1-6</sub>alkyl in rings of 5 or 6 or 7 members, where R<sup>b</sup> is C<sub>1-8</sub>alkylene or C<sub>2-8</sub>alkenylene, where R<sup>e</sup> is C<sub>2-8</sub>alkylene or C<sub>2-8</sub>alkenylene, where R<sup>c</sup> and R<sup>d</sup> are each independently H, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>3-6</sub>cycloalkyl or phenyl, or R<sup>c</sup> and R<sup>d</sup> taken

15 together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC<sub>1-6</sub>alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;

20 alternatively, R<sup>7</sup> may be taken together with an adjacent R<sup>4</sup> as well as their carbon and nitrogen of attachment to form a 5, 6 or 7 membered heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S, NH or NC<sub>1-6</sub>alkyl, and optionally and independently substituted with between 1 and 3 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;

25 R<sup>8</sup> and R<sup>9</sup> are, independently, H, F, Cl, Br, I, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -C<sub>3-6</sub>cycloalkyl, -OC<sub>3-6</sub>cycloalkyl, -OCH<sub>2</sub>Ph, -CF<sub>3</sub>, -OCF<sub>3</sub>, -SCF<sub>3</sub>, -(C=O)R<sup>k</sup> (wherein R<sup>k</sup> is H, C<sub>1-4</sub>alkyl, -OH, phenyl, benzyl, phenethyl or C<sub>1-6</sub>alkoxy), -(N-R<sup>t</sup>)(C=O)R<sup>k</sup> (where R<sup>t</sup> is H or C<sub>1-4</sub>alkyl), -(N-R<sup>t</sup>)SO<sub>2</sub>C<sub>1-4</sub>alkyl,

30 -(S(=O)<sub>p</sub>)-C<sub>1-4</sub>alkyl (wherein p is 0, 1 or 2), nitro, -SO<sub>2</sub>NR<sup>l</sup>R<sup>m</sup> (wherein R<sup>l</sup> and R<sup>m</sup> are independently selected from H, C<sub>1-4</sub>alkyl, phenyl, benzyl or phenethyl, or R<sup>l</sup> and R<sup>m</sup> taken together with the nitrogen to which they are

attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC<sub>1-4</sub>alkyl), -(C=O)NR<sup>l</sup>R<sup>m</sup>, cyano or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3

5 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy; and enantiomers, diastereomers and pharmaceutically acceptable salts and esters thereof,

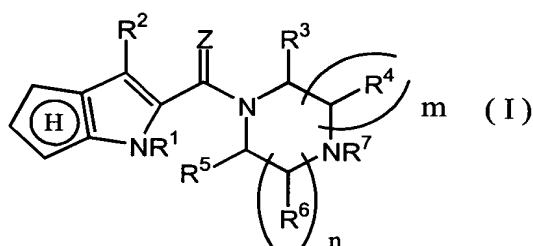
with the following provisos,

that R<sup>6</sup> adjacent to N must be H where R<sup>4</sup> adjacent to N is other than H,

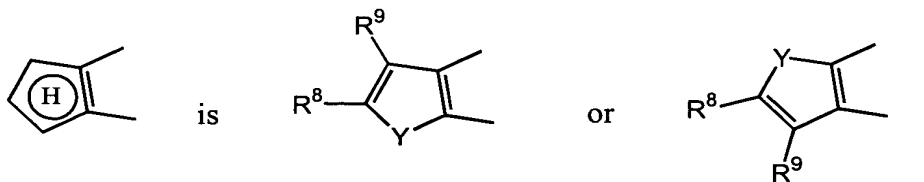
10 that R<sup>7</sup> is not -CH<sub>2</sub>CH<sub>2</sub>OH; and

that where the core molecule is a 4*H*-furo, then one of R<sup>4</sup> and R<sup>6</sup> adjacent to N must not be methyl when the other is hydrogen unless R<sup>6</sup> and R<sup>4</sup> are taken together to form a bridging moiety.

3 A method for the treatment or prevention of H<sub>4</sub>-mediated diseases and  
15 conditions comprising the step of administering to a patient in need of such treatment or prevention a pharmaceutical composition containing an effective amount of a compound of formula (I):



20 wherein



Y is O or S;

Z is O or S;

25 n is 1 or 2;

m is 1 or 2;

$n + m$  is 2 or 3;

$R^1$  is H or  $C_{1-6}$ alkyl;

$R^2$  is H, F, Cl, Br or  $C_{1-6}$ alkyl;

$R^3$  and  $R^4$  are, independently, H,  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl,

- 5  $C_{1-4}$ alkyl( $C_{3-6}$ cycloalkyl), cyano,  $-CF_3$ ,  $-(CO)NR^pR^q$ ,  $-(CO)OR^r$ ,  $-CH_2NR^pR^q$  or  $-CH_2OR^r$ ; where  $R^p$ ,  $R^q$  and  $R^r$  are independently selected from H,  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl, phenyl,  $-C_{1-2}$ alkyl( $C_{3-6}$ cycloalkyl), benzyl or phenethyl, or  $R^p$  and  $R^q$  taken together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional
- 10 heteroatoms selected from O, S, NH or  $NC_{1-6}$ alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from  $C_{1-3}$ alkyl, halo, hydroxy, amino, and  $C_{1-3}$ alkoxy;

$R^5$  and  $R^6$  are, independently, H or  $C_{1-6}$ alkyl;

- 15  $R^7$  is  $-R^a$ ,  $-R^bR^a$ ,  $-R^e-O-R^a$  or  $-R^e-N(R^c)(R^d)$ , where  $R^a$  is H, cyano,  $-(C=O)N(R^c)(R^d)$ ,  $-C(=NH)(NH_2)$ ,  $C_{1-10}$ alkyl,  $C_{2-8}$ alkenyl,  $C_{3-8}$ cycloalkyl,  $C_{4-7}$ heterocyclic radical or phenyl, where the  $C_{4-7}$ heterocyclic radical is attached at a carbon atom and contains one of O, S, NH or  $NC_{1-4}$ alkyl, and optionally an additional NH or  $NC_{1-6}$ alkyl in rings of 5 or 6 or 7
- 20 members, where  $R^b$  is  $C_{1-8}$ alkylene or  $C_{2-8}$ alkenylene, where  $R^e$  is  $C_{2-8}$ alkylene or  $C_{2-8}$ alkenylene, where  $R^c$  and  $R^d$  are each independently H,  $C_{1-4}$ alkyl,  $C_{2-4}$ alkenyl,  $C_{3-6}$ cycloalkyl or phenyl, or  $R^c$  and  $R^d$  taken together with the nitrogen to which they are attached, form a 4-7
- 25 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or  $NC_{1-6}$ alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from  $C_{1-3}$ alkyl, halo, hydroxy, amino, and  $C_{1-3}$ alkoxy;
- 30 alternatively,  $R^7$  may be taken together with an adjacent  $R^4$  as well as their carbon and nitrogen of attachment to form a 5, 6 or 7 membered heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S, NH or  $NC_{1-6}$ alkyl, and optionally and independently substituted with

between 1 and 3 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;

R<sup>8</sup> and R<sup>9</sup> are, independently, H, F, Cl, Br, I, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy,

5 -C<sub>3-6</sub>cycloalkyl, -OC<sub>3-6</sub>cycloalkyl, -OCH<sub>2</sub>Ph, -CF<sub>3</sub>, -OCF<sub>3</sub>, -SCF<sub>3</sub>, -(C=O)R<sup>k</sup>  
 (wherein R<sup>k</sup> is H, C<sub>1-4</sub>alkyl, -OH, phenyl, benzyl, phenethyl or C<sub>1-6</sub>alkoxy),  
 -(N-R<sup>t</sup>)(C=O)R<sup>k</sup> (where R<sup>t</sup> is H or C<sub>1-4</sub>alkyl), -(N-R<sup>t</sup>)SO<sub>2</sub>C<sub>1-4</sub>alkyl,  
 -(S(=O)<sub>p</sub>)-C<sub>1-4</sub>alkyl (wherein p is 0, 1 or 2), nitro, -SO<sub>2</sub>NR<sup>l</sup>R<sup>m</sup> (wherein R<sup>l</sup>  
 and R<sup>m</sup> are independently selected from H, C<sub>1-4</sub>alkyl, phenyl, benzyl or  
 phenethyl, or R<sup>l</sup> and R<sup>m</sup> taken together with the nitrogen to which they are  
 10 attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional  
 heteroatoms selected from O, S, NH or NC<sub>1-4</sub>alkyl), -(C=O)NR<sup>l</sup>R<sup>m</sup>, cyano  
 or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing  
 is optionally and independently substituted with between 1 and 3  
 substituents selected from C<sub>1-3</sub>alkyl, halo, hydroxy, amino, and C<sub>1-3</sub>alkoxy;

15 and enantiomers, diastereomers and pharmaceutically acceptable salts and  
 esters thereof,

with the following provisos,

that R<sup>6</sup> adjacent to N must be H where R<sup>4</sup> adjacent to N is other than H,

that R<sup>7</sup> is not -CH<sub>2</sub>CH<sub>2</sub>OH; and

20 that where the core molecule is a 4*H*-furo, then one of R<sup>4</sup> and R<sup>6</sup> adjacent to N  
 must not be methyl when the other is hydrogen unless R<sup>6</sup> and R<sup>4</sup> are taken  
 together to form a bridging moiety.